FXR MODULATORS

ABSTRACT OF THE DISCLOSURE

The present invention provides compounds, pharmaceutical compositions and methods that are useful in modulating the farnesoid X receptor (FXR). As FXR is involved in negatively controlling the expression level of cholesterol 7α-hydroxylase (*cyp*7a), the rate-limiting enzyme involved in the oxidative metabolism of cholesterol into bile acids, the compounds described herein find utility in treating diseases associated with abnormally high or low cholesterol levels. In certain aspects, the FXR modulators (*e.g.*, antagonists) described herein block the negative feed-back downregulation of *cyp*7a expression produced by certain cholic acids, the endogenous ligands for FXR. Moreover, as FXR forms heterodimers with the retinoid X receptor (RXR) in some cell types, modulation of the level of FXR activity in cells has a wide range of effects on a variety of biological processes which are mediated by RXR or other RXR-interacting proteins such as PPARγ and PPARα. Thus, compounds described herein are useful in treating other biological activities such as obesity, diabetes, lipid associated disorders, cancer, inflammatory disorders, disorders involving a disrupted or dysfunctional epidermal barrier, and various other metabolic disorders.